Conversion of *o*-Nitrothiophenols into *o*-Aminobenzenesulphonic Acids

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The mechanism of conversion of *o*-nitrothiophenols into *o*-aminobenzenesulphonic acids in aqueous dioxane has been investigated with particular reference to evidence for the rate-determining formation of a cyclic intermediate. This intermediate is susceptible to interception by both external and internal nucleophilic functions, and the sulphonic acid is shown by isotope labelling experiments to take *two* oxygen atoms from $H_2{}^{18}O$ in the reaction mixture, under conditions in which neither starting materials nor products exchange with $H_2{}^{18}O$. A tentative pathway is advanced.

o-Nitrothiophenol (**1a**), when kept in aqueous dioxane is converted in high yield into *o*-aminobenzenesulphonic acid (**2a**).

(1) (2)

(3) (4)

a; R = H; b; R = CONHEt; c; R = $CONH_2$; d; R = $CONEt_2$

Scheme 1.

This reaction offers a facile method and one superior to those previously employed[1] for the preparation of *o*-aminobenzenesulphonic acids valuable as dyestuff precursors. In this paper we report on the mechanism of this conversion.

The type of reaction was first observed by Veronese and his co-workers[2] in the conversion of 2-arylthiotryptophans into 2-hydroxytryptophans and in preliminary work[3] at I.C.I. Organics Division two principal observations, fully confirmed in the present work, were made: (i) the reaction is confined to *o*-nitrothiophenols; the fact that the *meta*- and *para*-isomers are inert strongly suggests an intramolecular interaction between these functions; (ii) water is essential for the reaction and is the source of oxygen in the sulphonic group. Under anhydrous conditions, the nitro-disulphide (**3a**) is slowly formed from 2-nitrothiophenol (**1a**).

Quantification of the Reaction and the Stoicheiometry of Water.—*o*-Nitrothiophenols are extremely easily oxidised and we have used a simple method for their *in situ* generation. Treatment of the appropriate *o*-halogeno-nitro compound with 2-cyanoethanethiolate gave the nitriles (**4**) which on treatment with base generated the thiolate ion from which the free thiol (**1**) was thereafter obtained by appropriate treatment. In typical experiments, the thiol was kept in aqueous dioxane under argon at *ca.* 85 °C and the progress of the reaction was monitored by h.p.l.c. It was established that disulphides (**3**) and sulphonic acids (**2**) were inert under the reaction conditions and do not react with the starting nitro-thiol.

Conversion of *o*-nitrothiophenol (**1a**) into the sulphonic acid (**2a**) is accompanied by formation of nitro-disulphide (**3a**). This is a reaction product and not an oxidation-derived impurity in the starting material; hence the importance of *in situ* generation of starting thiol. Results of Table 1 show the pattern of sulphonic acid and disulphide yields as a function of water concentration.

The following generalisations emerge from the results of Table 1. In the absence of water a very slow conversion into disulphide occurs and no sulphonic acid is formed. There is, therefore, no disproportionation pathway. Addition of 2 moles of water per mole of thiophenol produces a substantial increase in rate but appearance of sulphonic acid is very slow until water is in roughly five-fold molar excess (Table 1, Entry 4) over

Table 1. Conversion of 2-nitrothiophenol (**1a**) into 2-aminobenzenesulphonic acid (**2a**) and bis-2-nitrophenyl disulphide (**3a**)[a]

Entry	$[H_2O]$	$[H_2O]/[(1a)]$	k/s^{-1}	(**1a**) %	(**2a**) %	(**3a**) %	T/°C	$t_{min.}$
1	0	0	8×10^{-6} [b]	83.3	—	8.8	87	362
2	1.6×10^{-3}	2	1.2×10^{-5}	77.9	—	14.3	87	402
3	2.4×10^{-3}	3	—	74.7	4.5	16.1	87	370
4	4.0×10^{-3}	5	5.2×10^{-5}	26.5	16.7	20.4	87	375
5	8.3	8×10^{2}	9.4×10^{-5}	20.1	70.1	—	81	354
6	9.4	1.5×10^{3}	9.17×10^{-5}	13.2	82.5	—	81	364
7	9.4	1.5×10^{3}	9.06×10^{-5} [c]					
8	9.4	1.5×10^{3}	8.95×10^{-5} [d]					
9	9.4	1.5×10^{3}	9.21×10^{-5} [e]					
10	27.7	2.7×10^{3}	7.22×10^{-5}	16.0	76.5	4.1	81	381

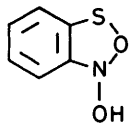
[a] All reactions under argon. [b] Approximate value. [c] In the dark. [d] 10 mol % *p*-dinitrobenzene. [e] 10 mol % galvinoxyl.

thiophenol. Further increase in the stoicheiometric water concentration produces little effect on the rate of conversion into sulphonic acid.

So far as products are concerned, in the absence of water or when it is present only in low concentrations, conversion into disulphide only is observed (Entries 1 and 2). At a molar ratio of five of water to one of (**1a**), disulphide and sulphonic acid are obtained in comparable amounts, but in the presence of large excesses of water (Entries 5—10) very little disulphide is obtained.

The co-existence of thiol and nitro groups in the same molecule provides an opportunity for single-electron-transfer (s.e.t.) reaction pathways. With this in mind, reactions have been performed with and without irradiation, in the presence of *p*-dinitrobenzene[4] as s.e.t. chain-transfer inhibitor and in the presence of galvinoxyl as radical trap. None of these variants of reaction conditions had any effect on the rate of disappearance of (**1a**).

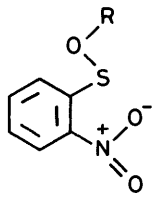
These observations suggested that juxtaposition of the nitro and thiol groups was required for reaction, that water was involved in the step that determined the rate of loss of thiol, and that radical intermediates were probably not involved. Initial formation of a cyclic isomer (**5**) as intermediate was regarded as



(**5**)

a possibility. This is the basis of the following discussion and further experiments.

Interaction between Functions and ortho-*Nitro Groups.*—Such interactions are familiar in a wide range of situations.[5] Particularly relevant in the present context is the ground-state structure of the sulphenate ester (**6a**)[6] which except for the alkyl



(**6**)

a; R = Me

b; R = –

group is strictly planar and with a sulphur–nitro group oxygen distance of 244 pm against a van der Waals radius sum of 325 pm.[7] These observations suggest a strong interaction between the *ortho* disposed functions and in addition the N–O bond of the S–O–N moiety is substantially longer than the other N–O bond. In this connection also, *o*-nitrobenzenesulphenate anion (**6b**) is considered to be stabilised by a sulphur–nitrogen interaction.[8]

From a kinetic standpoint, *o*-nitrobenzenesulphenyl chlorides[9] have been shown to undergo rapid exchange with $Li^{36}Cl$ in ethanoic acid but when the nitro group is not *ortho* to the sulphur function, exchange is slow. It was suggested that either the *ortho*-nitro group participated in an S–Cl dissociation or that a chloro-sulphurane was formed. Other observations on the kinetics of halogenation of sulphenyl halides[10] and of sulphenyl halides with alkenes[11] are likewise consistent with considerable interaction between the *ortho*-related groups.

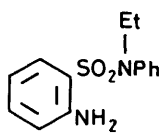
Table 2. Competition between water and *N*-ethylaniline in reaction with 2-nitrothiophenol (**1a**)

Nucleophile			Product %[a]		
PhNHEt[b]	H_2O[b]	k/s^{-1}[d]	(**2a**)	(**3a**)	(**7**)
0	10	4.3×10^{-6}[a]	94	5.2	—
1	9	—	62.2	3.3	29.0
3	7	—	29.3	1.7	70.7[c]
5	5	—	—	—	98.4
10	0	2.3×10^{-5}	—	—	97.8

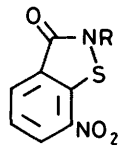
[a] With 5 moles per mole of nitrothiophenol. [b] Molar ratio with respect to (**1a**). [c] Makes more than 100%. [d] At 87 °C under Ar.

Evidence for ortho-*Interaction in the Nitro-thiol into Aminosulphonic Acid Conversion.*—We have drawn evidence from four lines of enquiry: (i) the reaction of external nucleophiles other than water, (ii) the effect of nucleophilic functions adjacent to the thiol group, (iii) the source of oxygen in the sulphonic acid product, (iv) the behaviour under the reaction conditions of compounds related to possible intermediates.

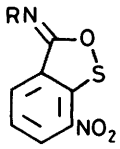
Competition between N-*Ethylaniline and Water as External Nucleophiles.*—In preliminary work,[3] it had been established that treatment of thiol (**1a**) with *N*-ethylaniline in the absence of water gave the aminobenzenesulphonamide (**7**). It was clearly of significance in relation to understanding the pathway of the



(**7**)



(**8**)



(**9**)

a; R = Et, b; R = H

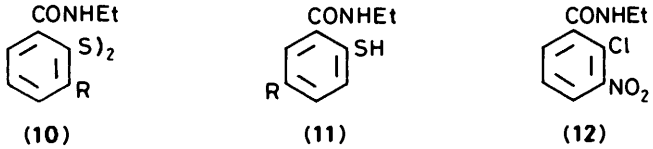
conversion of (**1a**) into (**2a**) to evaluate the competition between *N*-ethylaniline and water both in respect of the rate of consumption of nitro-thiol and the rate of formation of the respective products (**7**) and (**2a**) from the competition. The rate data (Table 2) show that replacement of water by *N*-ethylaniline produces only a five-fold increase in the rate of loss of nitro-thiol but that at equimolar amounts of water and amine as external nucleophiles, the water pathway to products is extinguished. *N*-Ethylaniline is undoubtedly more nucleophilic towards a wide range of electrophiles than is water[12] and these observations are consistent with loss of thiol being essentially independent of external nucleophile. Products on the other hand must be dependent on the nucleophilicity ratio, PhNHEt:H_2O, towards an intermediate along the pathway. It was established in separate experiments that sulphonamide (**7**) was not formed from sulphonic acid (**2a**) and amine under the reaction conditions. Formation of disulphide (**3a**) also appears to be suppressed when *N*-ethylaniline is the external nucleophile but amounts formed under any but completely anhydrous conditions (Table 1) are small.

Participation of Other Adjacent Functions in the Nitro-thiol.—Neighbouring amido groups have been particularly examined with reference to the participation of an adjacent substituent in the nitro-thiol amino-sulphonic acid conversion.

When (**1b**), generated *in situ* from (**4b**) (Scheme 1), was treated in aqueous dioxane under the standard reaction conditions, the

benzisothiazolone (**8a**) was obtained in 72% yield. Such a product is, of course, consistent with intramolecular attack by the mildly nucleophilic amido nitrogen atom on the sulphur atom of an intermediate such as (**5**). Under neutral conditions in intramolecular reactions, there is good evidence[13] that the oxygen atom of an amide is more nucleophilic than the nitrogen atom and rearrangement of a first formed intermediate such as (**9**) may be involved. By contrast, when the unsubstituted amide (**1c**) was submitted to the general reaction conditions, the products were the isothiazolone (**8b**) (41%) together with the sulphonic acid (**2c**) (35%). When amide (**1d**) was subjected to the reaction conditions, considerable decomposition occurred and the sulphonic acid (**2d**) (43%) was obtained.

It is to be noted that in none of the reactions in which an amido group could have participated in the reaction was any disulphide formed. The yields of disulphide formed from the parent thiol (**1a**) are of course very small except when the concentration of water is also small and very small yields may have been obtained. In this connection, we established that the disulphide (**10a**) was recovered essentially quantitatively under the reaction conditions and that the thiols (**11a** and **b**) were also stable in the reaction conditions. When, however, an attempt was made to obtain the disulphide (**10b**) by treatment of the chloride (**12**) with sodium disulphide, isothiazolone (**8a**) was



(**10**) (**11**) (**12**)

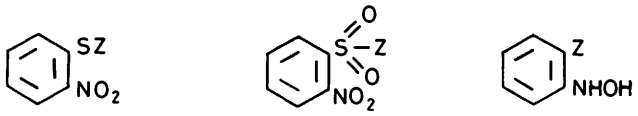
a; R = H
b; R = NO_2

obtained in 60% yield but no other recognisable products. It appears therefore that intramolecular attack of an amido group on sulphur is called into play by a neighbouring nitro-group and this suggests an intermediate other than disulphide on the pathway to thiazolone.

The Source of Oxygen in the Product Sulphonic Acid.—It was very difficult to establish the stoicheiometry with respect to water because reactions in which water concentrations were reduced to stoicheiometric amounts were very slow. We accordingly examined the conversion of (**1a**) into (**2a**) in dioxane in the presence of a 17-fold molar excess of $H_2{}^{18}O$. Mass-spectral examination of the sulphonic acid obtained showed that incorporation of *two* oxygen atoms from the water had occurred. It was important to establish whether or not the starting material or product was susceptible to oxygen exchange under the reaction conditions. The small-scale recovery of nitro-thiol (**1a**) was not attempted but instead it was shown that *o*-dinitrobenzene did not undergo exchange under the reaction conditions and neither did the product sulphonic acid (**2a**).

Involvement of Intermediates in the Nitro-thiol into Sulphonic Acid Conversion.—In view of the transfer of oxygen to sulphur in the reaction and the strong evidence for the intramolecular nature of such transfer, we examined certain candidate compounds for the possibility that they could lie on the reaction pathway.

The free sulphenic acid (**13b**) has not been described and attempts to isolate it directly from the hydrolysis of the chloride (**13a**) failed. When an equivalent of the chloride (**13a**) and aqueous sodium hydroxide were kept in dioxane under the standard conditions for the nitro-thiol into aminobenzenesulphonic acid conversion, h.p.l.c. showed rapid conversion into the disulphide and sulphinic acid (**14a**) together with a third component with a longer retention time (less polar component). In a separate experiment at 20 °C, it was found that treatment of the sulphenyl halide (**13a**) with 1.2 molar equivalents of aqueous sodium hydroxide gave the disulphide and sulphinic acid (**14a**) in the ratio of 1:3.



(**13**) (**14**) (**15**)

a; Z = Cl **a**; Z = H **a**; Z = H
b; Z = OH **b**; Z = CH_2Ph **b**; Z = SO_2H

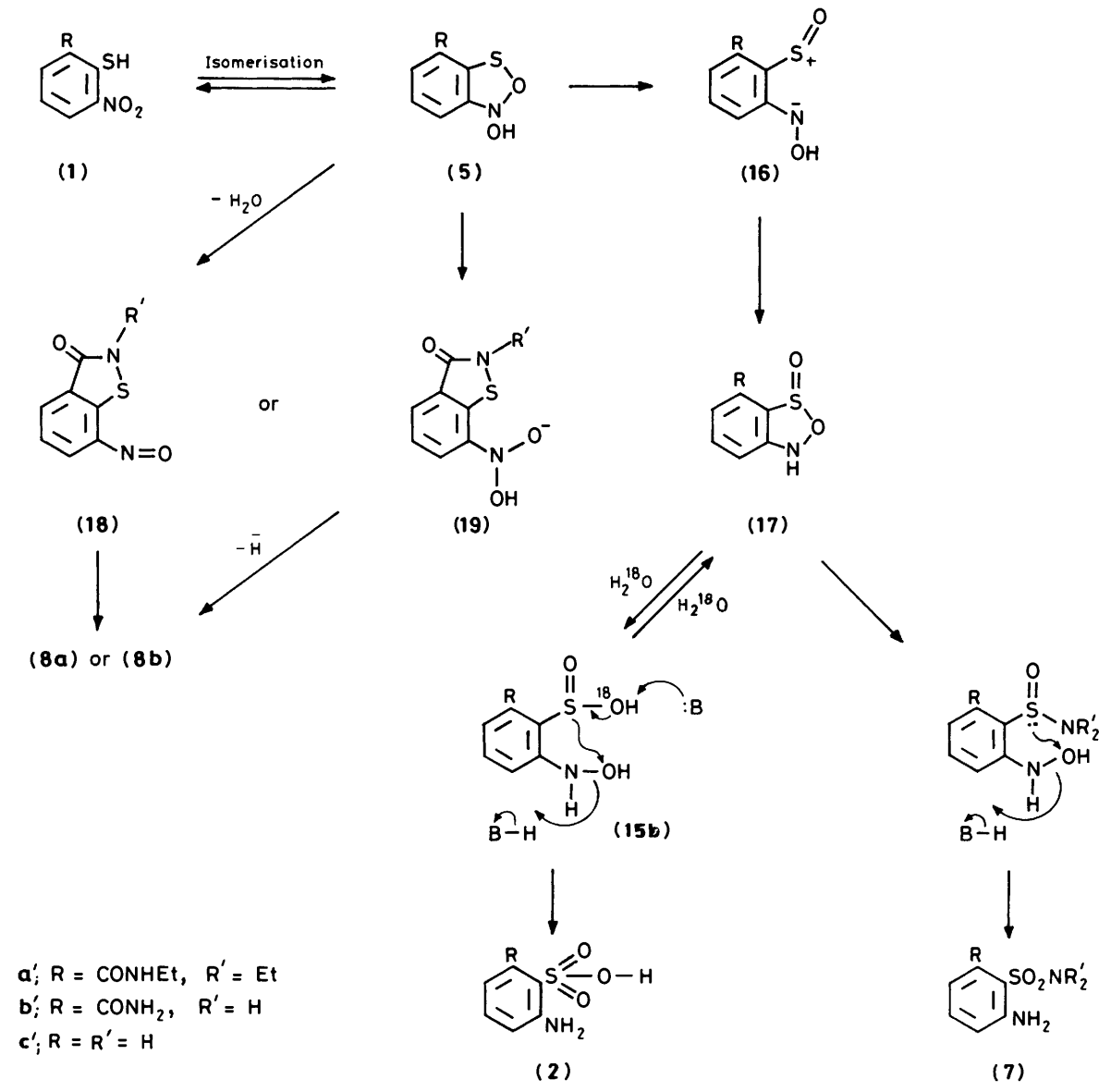
Sulphinic acid (**14a**), when subjected to the standard reaction conditions, underwent slow desulphination to give nitrobenzene with a half-life considerably greater than the thiol into sulphonic acid conversion. No conversion into sulphonic acid was detectable by h.p.l.c. We consider that these experiments rule out both (**13b**) and (**14a**) as intermediates in the reaction under discussion. Interestingly, when sulphinic acid (**14a**) was heated under the standard reaction conditions in the presence of $H_2{}^{18}O$, and recovered sulphinic acid was converted into the sulphone (**14b**), mass spectrometry showed 76% incorporation of one ^{18}O and some double incorporation. In view of the evidence below we think that ^{18}O is incorporated during equilibriation of (**17**) into (**20**) or directly into (**20**).

In view of oxidation at sulphur being accompanied by reduction at nitrogen, we considered the involvement of hydroxylamines similar to the putative intermediate (**5**). *N*-Phenylhydroxylamine (**15a**) was itself essentially stable under the reaction conditions, being recovered in 84% yield after two half-lives, and showing no oxygen exchange in the presence of $H_2{}^{18}O$. The sulphinic acid (**15b**) has not been described and we attempted *in situ* generation by reduction of sulphinic acid (**14a**), under the standard conditions (zinc and ammonium chloride) for conversion of nitroarenes into arylhydroxylamines. We failed to isolate (**15b**) but when the reduction mixture was subjected to the standard conditions for nitro-thiol into sulphonic acid conversion, the aminobenzenesulphonic acid (**2a**) was obtained in 76% yield. The observation of an oxygen-transfer product under *reducing* conditions is striking and, we think, lends support to the tentative involvement of (**15b**) on the pathway between (**1a**) and (**2a**).

We have also considered the possibility that intermediates with a three-co-ordinate sulphur atom linked to oxygen, such as (**17**), might be susceptible to deoxygenation. Triphenylphosphine, for example, is well known to deoxygenate sulphoxides.[14] When 2-nitrothiophenol was submitted to the standard conditions but in the presence of an equimolecular amount of triphenylphosphine, the yield of sulphonic acid (**2a**) was reduced to 50% and triphenylphosphine oxide was obtained in 16% yield. Nitrobenzene does not convert triphenylphosphine into triphenylphosphine oxide under the standard conditions and again the possibility that a three-co-ordinate sulphur-containing species is an intermediate is supported.

Conclusions

The evidence that we have so far collected on this deceptively simple reaction may be summarised with reference to Scheme 2. The conversion of (**5**) into (**2**) *via* (**16**) and (**17**) is, of course, speculative. It does, however, account for the incorporation of two *but not more* heavy oxygen atoms from $H_2{}^{18}O$ in the course of the reaction. This suggests therefore that one of the nitro



Scheme 2.

group oxygen atoms is retained past intermediate (**17**). We have to suggest, without direct evidence, either that a nitrosoisothiazolone (**18**) is formed by dehydration on the pathway to nitroisothiazolones (**8**) and is subsequently oxidised or that oxidation of (**18**) regenerates the nitro group. Competition between the external nucleophiles, water and *N*-ethylaniline, appears to occur with intermediate (**17**). A related scheme, which was advanced[15] before the results of ^{18}O labelling studies were known, has been discussed earlier by one of us. This scheme, as the present one, takes into account the potential reversibility of some of the steps.

Experimental

Solids were crystallised to a constant m.p. Light petroleum refers to the fraction b.p. 40—60 °C. Extracts were dried over Na_2SO_4. H.p.l.c. was performed using Waters Associates equipment on a Lichrosorb RP 2 column with MeCN–H_2O–$Bu_4N^+Br^-$–$MeCO_2H$ in the ratio 50:45:5:0.05 with a flow rate of 1 ml min^{-1} or (reverse phase) RPC 8 with MeOH–CH_2Cl_2 (9:1). G.c.–m.s. were determined on a Finnegan 1020 instrument. Dioxane was refluxed over sodium and distilled before use. $H_2{}^{18}O$ was 50.4% enriched. 2-Nitrothiophenol was obtained by reaction of 2-chloronitrobenzene with sodium sulphide nonahydrate in dimethyl sulphoxide. It had m.p. 57 °C (from chloroform–light petroleum) (lit.,[16] m.p. 56.5 °C).

Conversion of 2-*Nitrothiophenol* (**1a**) *into* 2-*Aminobenzenesulphonic Acid* (**2a**).—2-Nitrothiophenol (1.5 g, 9 mmol) in aqueous dioxane (19:1 v/v) (60 ml) was kept under oxygen-free nitrogen at 87 °C for 8 h. The suspension was cooled to 55 °C and filtration gave 2-aminobenzenesulphonic acid (1.45 g, 87%), m.p. 315 °C (decomp.) (Found: C, 41.5; H, 4.1; N, 8.1. Calc. for $C_6H_7NO_3S$: C, 41.6; H, 4.0; N, 8.1%); *m/z* 173 with abundant fragments at 155, 93, and 91 all identical with an authentic specimen, m.p. 320 °C (decomp.). The mother liquors on evaporation gave 2,2'-dinitrodiphenyl disulphide (0.13 g, 7%), m.p. and mixed m.p. 197—198 °C, i.r. spectrum identical with that of an authentic specimen.

Both sulphonic acid and disulphide were recovered in >90% yields when subjected to the reaction conditions.

When 2-nitrothiophenol (170 mg, 1.1 mmol) in aqueous dioxane (19:1 v/v) (6.8 ml) was treated with triphenylphosphine (300 mg, 1.1 mol) and the mixture was kept under argon at 87 °C for 12 h, crystals of 2-aminobenzenesulphonic acid (96 mg, 50.4%), m.p. >320 °C (i.r. identical with authentic specimen) separated. T.l.c. ($CHCl_3$–light petroleum, 9:1) showed triphenylphosphine, triphenylphosphine oxide, and five other components. The mother liquor was evaporated to dryness and the residue on treatment with chloroform–light petroleum gave triphenylphosphine oxide (54 mg), m.p. and mixed m.p. 154—155 °C, i.r. identical with an authentic specimen.

Nitrobenzene was treated with triphenylphosphine in aqueous dioxane under the standard conditions under argon for 16 h. No triphenylphosphine oxide (t.l.c.) was obtained and nitrobenzene was recovered quantitatively (g.l.c.)

In situ *Generation of* 2-*Nitrothiophenol*.—2-Nitrothiophenol (5.8 mmol) in hexamethylphosphoramide (HMPA) (7 ml) was treated with 3-chloropropiononitrile (7 mmol) and lithium hydroxide (6.0 mmol). After being stirred at 42 °C for 36 h under N_2, the mixture was diluted with water (100 ml) and the precipitate (1.0 g, 83%), m.p. 68—72 °C, was filtered off. Crystallisation gave the pure *sulphide* (**4a**) (74%), m.p. 74 °C (from dichloromethane–light petroleum) (Found: C, 51.7; H, 3.9; N, 13.3. Calc. for $C_9H_8N_2O_2S$: C, 51.9; H, 3.8; N, 13.5%) (lit.,[17] m.p. 78 °C).

The sulphide (0.72 mmol) in dioxane (5 ml) was treated with sodium hydroxide (1.44 mmol) in water (2.28 ml). After 20 min, the mixture was diluted with dioxane–acetonitrile–water (2:1:5) (34 ml), the pH was adjusted to 4.9 with HCl, and the whole made up to 50 ml with water. H.p.l.c. showed the yield of 2-nitrothiophenol to be 86%.

Experiments with $H_2{}^{18}O$.—(a) 2-*Nitrothiophenol*. The thiol (50 mg) in dioxane (1.9 ml) was treated with water ($H_2{}^{18}O$) (100 μl) and the mixture was kept at 87 °C under nitrogen for 8 h. The precipitate was filtered off, washed with hot dioxane, and dried under reduced pressure at 88 °C to constant weight. The mass spectrum shows a strong peak at *m/z* 93 and weak peaks at *m/z* 173, 175, and 177 in the ratio 1:2:1. With isotopically normal water the molecular ion was 173 with no higher molecular mass peaks.

(b) 1,2-*Dinitrobenzene* (0.68 g) was recovered (0.62 g, 91%) from treatment in the standard reaction conditions for 12 h. When $H_2{}^{18}O$ was used the mass spectrum showed an isotopically normal molecular ion.

(c) 2-*Aminobenzenesulphonic acid* under the standard reaction conditions gave recovered material with an isotopically normal molecular ion.

(d) N-*Phenylhydroxylamine*. The amine (27 mg) was kept with $H_2{}^{18}O$ (50 μl) in dioxane (250 μl) at 87 °C for 5.5 h. Evaporation to constant weight at 60 °C/18 mmHg and mass spectrometric analysis of the residue showed the molecular ion at *m/z* 109. I.r. spectrum was identical with starting material. On a larger scale (750 mg) there was a slow conversion into a less polar product (h.p.l.c.) but after 6 h, 82% of the starting material was recovered.

In situ *Generation and Reaction of* 2-(N-*Ethylcarbamoyl*)-6-*nitrothiophenol* (**1b**).—2-Chloro-3-nitrobenzoic acid[18] was converted into the acid chloride with thionyl chloride and treatment of the product (0.5 g) with ethylamine (1 mol) in toluene gave the *ethylamide* (0.45 g, 88%), m.p. 111 °C (from methanol) (Found: C, 46.7; H, 3.8; H, 11.9. $C_9H_9ClN_2O_3$ requires C, 47.3; H, 3.9; N, 12.3%). The amide (0.22 mmol) was treated with 2-cyanoethanethiol[19] (0.22 mmol) and lithium hydroxide (0.22 mmol) in HMPA (10 ml) under argon at 45—50 °C for 4 h. Dilution with water and extraction with diethyl ether gave the *amido-sulphide* (**4b**) (34 mg, 55%), m.p. 106 °C (from dichloromethane–light petroleum) (Found: C, 57.3; H, 4.8; N, 17.1. $C_{12}H_{13}N_3O_3S$ requires C, 58.0; H, 5.2; N, 17.0%).

The sulphide (0.609 mmol) in aqueous dioxane (7:3 v/v) (10 ml) was treated with sodium hydroxide (0.73 mmol) in water (243 μl) under argon. The mixture was acidified to pH 5.7 with HCl and then kept at 87 °C for 6 h. Evaporation to dryness gave N-*ethyl*-7-*nitrobenz*[d]*isothiazol*-3(2H)-*one* (**8a**) (0.091 g, 67%) m.p. 121 °C (0.054 g) (from chloroform–light petroleum) (Found: C, 47.8; H, 3.7; N, 12.3. $C_9H_8N_2O_3S$ requires C, 48.2; H, 3.6; N, 12.5%); *m/z* M^+ 224; $\nu_{C=O}$ 1 670s and $\nu(NO_2)$ 1 510 and 1 310 cm^{-1}; $\delta(CDCl_3$; TMS; 60 HHz) 8.5 (t, 2 H), 7.6 (t, 1 H), 4.0 (q, 2 H), and 1.4 (t, 3 H).

In situ *Generation and Reaction of* 2-*Carbamoyl*-6-*nitrothiophenol* (**1c**).—2-Chloro-3-nitrobenzamide (0.3 g, 1.5 mmol) was treated with 2-cyanoethanethiol in HMPA as described in the preceding section. The *sulphide* (**4c**) (0.22 g, 75%) had m.p. 102 °C (from dichloromethane–light petroleum) (Found: C, 47.9; H, 3.7; N, 16.4; S, 13.0. $C_{10}H_9N_3O_3S$ requires C, 47.8; H, 3.6; N, 16.7; S, 12.8%).

The sulphide (0.15 g, 6 mmol) was treated with aqueous sodium hydroxide in dioxane as for sulphide (**4b**) above. The generated thiol, subjected to the standard conditions, gave a mixture (0.091 g) which on crystallisation from chloroform–light petroleum separated into first, 2-*amino*-6-*carbamoylbenzenesulphonic acid* (**2c**) (0.042 g, 33%), m.p. 230—235 °C (Found: C, 38.6; H, 3.6; N, 12.9. $C_7H_8N_2O_4S$ requires C, 38.9; H, 3.7; N, 13.0%); $\nu_{C=O}$ 1 690s cm^{-1}; *m/z* M^+ 216. Positive test with Erhlich's reagent. The second fraction was 7-*nitrobenz*[d]-*isothiazol*-3(2H)-*one* (0.045 g, 38%), m.p. 147 °C (Found: C, 41.9; H, 2.0; N, 14.3. $C_7H_4N_2O_3S$ requires C, 42.9; H, 2.0; N, 14.2%); i.r. $\nu_{C=O}$1 710s, and 1 550 and 1 320 $cm^{-1}(NO_2)$; *m/z* M^+, 196.

In situ *Generation and Reaction of* 2-(N,N-*Diethylcarbamoyl*)-6-*nitrothiophenol* (**1d**).—Treatment of 2-chloro-3-nitrobenzoyl chloride with diethylamine (2 mol equiv.) in toluene as before gave the *amide* (0.5 g, 86%), m.p. 59 °C (Found: C, 50.7; H, 4.9; N, 11.1. $C_{11}H_{13}ClN_2O_3$ requires C, 51.5; H, 5.1; N, 10.9%). The amide (600 mg) with 2-cyanoethanethiol and lithium hydroxide in HMPA as before gave the *sulphide* (**4d**) (370 mg, 57%), m.p. 53.0 °C (Found: C, 62.0; H, 6.15; N, 15.3. $C_{14}H_{17}N_3O_3S$ requires C, 61.1; H, 6.2; N, 15.3%). Treatment of the sulphide (90 mg) with sodium hydroxide in dioxane as before and subsequent thermolysis of the liberated thiol, which occurred with considerable decomposition, gave crude *sulphonic acid* (**2d**) (51 mg) with m.p. 174 °C (decomp.) (32 mg) after crystallisation from methanol (Found: C, 48.2; H, 5.7; N, 10.3. $C_{11}H_{16}N_2O_4S$ requires C, 48.5; H, 5.9; N, 10.3%); $\nu_{C=O}$ 1 675s; *m/z* M^+ 272. Positive Erhlich's test.

2-(N-*Ethylcarbamoyl*)-4-*nitrothiophenol* (**11b**).—Dropwise addition of ethylamine (0.2 g) in anhydrous toluene (10 ml) to 2-chloro-5-nitrobenzoyl chloride (0.5 g) in toluene (7 ml), subsequent addition of water, and extraction with dichloromethane gave the *amide* (0.43 g, 81%), m.p. 122 °C (Found: C, 46.6; H, 3.9; N, 11.8. $C_9H_9ClN_2O_3$ requires C, 47.3; H, 3.9; N, 12.3%).

The preceding amide (1 g) was kept with sodium sulphide (1.25 mol equiv.) in DMSO at 45 °C. Working up was by addition to ice–water, filtration, and dissolution of the precipitate in chloroform. The *thiol* (0.69 g, 69%) had m.p. 93 °C (from chloroform); $\nu_{max.}(NO_2)$ 1 510 and 1 350 cm^{-1} (Found: C, 47.1; H, 4.4; N, 13.9. $C_9H_{10}N_2O_3S$ requires C, 47.8; H, 4.4; N, 14.2%); *m/z* M^+ 226.

The thiol (0.5 g) was kept in aqueous dioxane under the standard conditions at 87 °C for 7 h. The mixture was evaporated to dryness and flash chromatography (CH_2Cl_2–light

petroleum 1:1) separated first, 2,2′-*bis*-(N-*ethylcarbamoyl*)-4,4′-*dinitrodiphenyl disulphide* (150 mg), m.p. 245 °C; *m/z* M^+ 450. The second component was recovered thiol (310 mg), m.p. and mixed m.p. 93 °C.

(Note: The amido-nitro compounds described above gave consistently low carbon analyses. All other criteria indicated pure compounds of the assigned structures.)

Reactivity of 2-*Nitrobenzenesulphinic Acid* (**14a**).—The acid[20] (200 mg) was kept in aqueous dioxane (5:2 v/v) (40 ml) at 87 °C for 6 h. H.p.l.c. (Lichrosorb RP 2) showed that decrease in the acid peak R_T 4.40 was matched by appearance of a peak at R_T 6.50 identical with that of nitrobenzene. No 2-aminobenzenesulphonic acid (R_T 4.52), 2-nitrothiophenol (R_T 7.30), or 2,2′-dinitrodiphenyl disulphide (R_T 16.76) was observed.

The acid (1 g) was heated in dioxane (10 ml) containing $H_2{}^{18}O$ (100 μl) at 86 °C for 5.5 h under argon. Evaporation to dryness and neutralisation of the residue with aqueous sodium carbonate gave the sodium salt (0.64 g) which was washed with cold ethanol, dried under reduced pressure, and then treated with benzyl bromide (1.04 g) at 80 °C for 7 h. Addition of water and extraction with ether gave benzyl 2-nitrophenyl sulphone (0.88 g), m.p. 124 °C (Found: C, 56.0; H, 3.7; N, 4.9. Calc. for $C_{13}H_{11}NO_4S$: C, 56.3; H, 4.0; N, 5.1%) (lit.,[21] m.p. 127—128 °C).

Attempted in situ *Generation of* 2-*Hydroxyaminobenzenesulphinic Acid* (**15b**).—2-Nitrobenzenesulphinic acid (907 mg) and ammonium chloride (250 mg) in aqueous dioxane (5:2 v/v) (15 ml) were stirred vigorously at 20 °C. Zinc powder (620 mg) was added during 10 min with the temperature maintained at 60—65 °C. Stirring was continued for 20 min after addition was complete and the pH was then adjusted to 4.5. The mixture was then kept at 87 °C under argon for 7 h, filtered, and the filtrate evaporated to dryness. Trituration with methanol afforded 2-aminobenzenesulphonic acid (540 mg), m.p. 320 °C (decomp.), undepressed on admixture with an authentic specimen whose i.r. spectrum was identical. Mass spectral data showed a molecular ion at *m/z* 173. No other products were identified.

Kinetics.—Solvents were degassed before use. In a typical run, 2-nitrothiophenol (78 mg) in aqueous dioxane (5:2 v/v) (50 ml) was kept at 81 °C under argon and 2 ml aliquots were removed at intervals of *ca.* 40 min over 6 h. The aliquots were diluted with acetonitrile–water (8.5:1.5 v/v) and 10 μl portions were injected onto a 30 cm Lichrosorb RP2 column with mobile phase MeCN–H_2O–$Bu_4N^+Br^-$ (0.79M)–$MeCO_2H$ (50:45:5:0.05) and flow rate 1 ml min^{-1}. The R_T values for (**1a**), (**2a**), and (**3a**) were 7.73, 4.50, and 18.54 min respectively. The concentrations of the components of each aliquot were determined by reference to known mixtures of authentic materials. Plots of $\log_e$ [(**1a**)] were linear with *t* but not the corresponding plots of $\log_e$ [(**2a**)] or $\log_e$ [(**3a**)].

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